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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/540,634	04/19/2006	Gert Jules Hector De Wilde	D0590.70034US01	8371

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EXAMINER	
LEE, JAE W	

ART UNIT	PAPER NUMBER
1656	

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Please find below and/or attached an Office communication concerning this application or proceeding.

The time period for reply, if any, is set in the attached communication.

Office Action Summary	Application No.	Applicant(s)	
	10/540,634	DE WILDE, GERT JULES HECTOR	
	Examiner	Art Unit	
	Jae W. Lee, Ph.D.	1656	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 February 2007*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-29* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *06/23/2005* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date *11/10/2005*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Application status

Preliminary amendments for specification and claims, filed on 06/23/2005, are acknowledged. In the amendment, filed on 06/23/2005, Applicants have canceled claims 1-17 and added claims 18-29.

Claims 18-29 are pending in this application.

Priority

A claim of priority to the PCT/EP03/14674, filed on 12/19/2003, US Provisional Application No. 60/436,380, filed on 12/23/2002, and the Foreign Application UNITED KINGDOM 0230014.3, filed on 12/23/2002, is acknowledged.

Election

Applicant's species election of SEQ ID NO: 3 encoding SEQ ID NO: 4, is acknowledged. Applicants did not provide any argument for the traversal, therefore, it will be considered as an election without traverse.

SEQ ID NOs: 1, 2, 5-10 are withdrawn from further consideration by the Examiner, 37 CFR 1.142(b) as being drawn to a non-elected invention.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim

remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Objections to the Specification

The specification is objected to because descriptions of Figures do not have a proper heading, "Brief Description of Drawings," according to M.P.E.P. 608.01(f). Instead, in the instant application, the descriptions of Figures are under an improper heading, "In the Figures:"

The specification is objected to for inappropriate notation of an Internet address. On page 5, 6, 31 and 40, Internet address is cited in an unacceptable form. See M.P.E.P. 707.05(e) for the acceptable notation of an Internet address. The examiner suggests the replacement of Internet citations with appropriate references because Internet pages are subjected to frequent changes and deletions and could be different when the public accesses the Internet page to view the exactly same information.

This application contains sequence disclosures that are encompassed by the definitions for nucleotide and/or amino acid sequences set forth in 37 CFR 1.821(a)(1) and (a)(2). However, this application fails to comply with the requirements of 37 CFR 1.821 through 1.825; Applicants' attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). To be in compliance, Applicants should identify nucleotide sequences of at least 10 nucleotides and amino acid sequences of at least 4 amino acids in the specification by a proper sequence identifier, i.e., "SEQ ID NO:" (see MPEP 2422.01). If these sequences have

not been listed in the computer readable form and paper copy of the sequence listing, applicant must provide an initial computer readable form (CRF) copy of the "Sequence Listing", an initial paper copy of the "Sequence Listing", as well as an amendment directing its entry into the specification, and a statement that the content of the paper and CRF copies are the same and, where applicable, include no new matter as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.821(b) or 1.825(d). In the instant application, a statement, that the content of the paper and CRF copies are the same, is missing.

Appropriate correction for each error is required.

Claim Objections

Claims 20, 21, 23, 24, 26, 27 and 29 are objected to because of the following informalities:

Claims 20, 21, 23, 26, 27 and 29 are objected for containing non-elected subject matters, i.e., SEQ ID NOs: 1, 2 and 5-10.

Claim 24 is objected to because the phrase, "which nucleic acid sequence or ortholog expresses." The Examiner suggests the following phrase, --- which said nucleic acid sequence or said ortholog expresses ---, to the extent that it is Applicant's intent.

Appropriate correction is required.

Claim Rejections - 35 U.S.C. § 112

The following is a quotation of the second paragraph of 35 U.S.C. § 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 18, 20, 21, 24, 26, 27 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claim 18 is unclear because it is unclear whether "the signal generated" in step b) is a result of a test chemical or a compound. It is unclear whether a test chemical and a compound are used interchangeably or whether they are separate entities.

Claims 18, 20, 21, 24, 26, 27 recite the phrase, "T17E9.1a/*kin-18*," which is unclear. It is unclear with respect to what is encompassed by the phrase.

Claim 24 recites the limitation "said protein" in Claim 24. There is insufficient antecedent basis for this limitation in the claim.

The following is a quotation of the first paragraph of 35 U.S.C. § 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claims 18-29 are rejected under 35 U.S.C. § 112, first paragraph, written description, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to

reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

Claims 18-29 are drawn to a genus of methods for identifying a compound useful in the prevention and/or treatment of metabolic diseases, comprising the steps of: a) contacting any protein encoded by any T17E9.1a/*kin-18* gene or any ortholog thereof with a test chemical, in such a way that any signal is generated that is representative for the interaction between said test chemical and said protein; and b) detecting the signal thus generated, said signal identifying a compound that modulates said protein or polypeptide, which is indicative that the compound is useful for the prevention and/or treatment of metabolic diseases.

To satisfy the written description aspect of 35 U.S.C. § 112, first paragraph, for a claimed genus of [compositions or methods], it must be clear that: (1) the identifying characteristics of the claimed [compositions or methods] have been disclosed, e.g., structure, physical and/or chemical characteristics, functional characteristics when coupled with a known or disclosed correlation between function and structure, or a combination of these; and (2) a representative number of species within the genus must be disclosed.

The specification discloses an example of a method for screening 96 commercially available kinase inhibitors to test which of them modulates the kinase activity of a protein having the amino acid sequence of SEQ ID NO: 4 (human JIK protein) using the commercially available Kinase Glo® Luminescent Kinase Assay (Promega, USA). However, this is an inadequate written description for a genus of

methods for identifying a compound useful in the prevention and/or treatment of metabolic diseases, comprising the steps of: a) contacting any protein encoded by any T17E9.1a/*kin-18* gene or any ortholog thereof with a test chemical, in such a way that any signal is generated that is representative for the interaction between said test chemical and said protein; and b) detecting the signal thus generated, said signal identifying a compound that modulates said protein or polypeptide, which is indicative that the compound is useful for the prevention and/or treatment of metabolic diseases.

The genus of claimed methods is not supported by the specification because there is no disclosure of any particular structure to function/activity relationship between any protein encoded by T17E9.1a/*kin-18* gene or any ortholog thereof, and the desired function/activity of said protein in the claimed methods, wherein such function/activity is required to produce a signal when there is an interaction between a compound being screened and said protein. The specification also lacks description with respect to what function, if there is any, is required for any protein encoded by T17E9.1a/*kin-18* gene or any ortholog thereof. Further, the specification fails to describe any identification of structural characteristics or properties of "any ortholog thereof" that encodes any homologous protein encoded by any T17E9.1a/*kin-18* gene. Given the lack of additional representatives of a genus of methods for identifying a compound useful in the prevention and/or treatment of metabolic diseases, comprising the steps of: a) contacting any protein encoded by any T17E9.1a/*kin-18* gene or any ortholog thereof with a test chemical, in such a way that any signal is generated that is representative for the interaction between said test chemical and said protein; and b) detecting the signal

thus generated, said signal identifying a compound that modulates said protein or polypeptide, which is indicative that the compound is useful for the prevention and/or treatment of metabolic diseases as encompassed by the claim, Applicants have failed to sufficiently describe the claimed invention, in such full, clear, concise, and exact terms that a skilled artisan would recognize Applicants were in possession of the claimed invention.

Applicant is referred to the revised guidelines concerning compliance with the written description requirement of U.S.C. 112, first paragraph, published in the Official Gazette and also available at www.uspto.gov.

Claims 18-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement, because the specification, while being enabling for a method for screening 96 commercially available kinase inhibitors to test which of them modulates the kinase activity of a protein having the amino acid sequence of SEQ ID NO: 4 (human JIK protein) using the commercially available Kinase Glo® Luminescent Kinase Assay (Promega, USA), does not reasonably provide enablement for any method for identifying a compound useful in the prevention and/or treatment of metabolic diseases, comprising the steps of: a) contacting any protein encoded by any T17E9.1a/*kin-18* gene or any ortholog thereof with a test chemical, in such a way that any signal is generated that is representative for the interaction between said test chemical and said protein; and b) detecting the signal thus generated, said signal identifying a compound that modulates said protein or polypeptide, which is

indicative that the compound is useful for the prevention and/or treatment of metabolic diseases. Therefore, the specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention commensurate in scope with these claims.

The factors to be considered in determining whether undue experimentation is required are summarized In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988). The Court in Wands states: "Enablement is not precluded by the necessity for some experimentation such as routine screening. However, experimentation needed to practice the invention must not be undue experimentation. The key word is 'undue,' not 'experimentation.' " (Wands, 8 USPQ2d 1404). Clearly, enablement of a claimed invention cannot be predicated on the basis of quantity of experimentation required to make or use the invention. "Whether undue experimentation is needed is not a single, simple factual determination, but rather is a conclusion reached by weighing many factual considerations." (Wands, 8 USPQ2d 1404). The factors to be considered in determining whether undue experimentation is required include: (1) the quantity of experimentation necessary, (2) the amount or direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. While all of these factors are considered, a sufficient amount for a *prima facie* case is discussed below.

Claims 18-29 are so broad as to encompass any method for identifying a compound useful in the prevention and/or treatment of metabolic diseases, comprising

the steps of: a) contacting any protein encoded by any T17E9.1a/*kin-18* gene or any ortholog thereof with a test chemical, in such a way that any signal is generated that is representative for the interaction between said test chemical and said protein; and b) detecting the signal thus generated, said signal identifying a compound that modulates said protein or polypeptide, which is indicative that the compound is useful for the prevention and/or treatment of metabolic diseases.

The claims rejected under this section of U.S.C. 112, first paragraph, do not place any structural limits on the "protein encoded by any T17E9.1a/*kin-18* gene or any ortholog thereof " in the claimed methods. Since the amino acid sequence of a polypeptide determines its structural and functional properties, predictability of which polypeptides can be used while obtaining the desired function requires a knowledge of and guidance with regard to which amino acids in the polypeptide's sequence, if any, are conserved (i.e. expectedly intolerant to modification), and detailed knowledge of the ways in which the polypeptide's structure relates to its desired function. In addition, the scope of the claims is not commensurate with the enablement provided by the disclosure with regard to the extremely large number of different peptides/proteins. The specification, however, only discloses two polypeptides having the amino acid sequences of SEQ ID NO: 4 and SEQ ID NO: 8 in the specification on page 43.

While recombinant and mutagenesis techniques are known, it is not routine in the art to screen for multiple substitutions or multiple modifications, as encompassed by the instant claims, and the positions within a protein's sequence where amino acid modifications can be made with a reasonable expectation of success in obtaining the

desired activity/utility are limited in any protein and the result of such modifications is unpredictable. In addition, one skilled in the art would expect any tolerance to modification for a given protein to diminish with each further and additional modification, e.g. multiple substitutions.

The specification does not support the broad scope of the claims which encompass 1) contacting all modifications and fragments of any protein encoded by any T17E9.1a/*kin-18* gene or any ortholog thereof with a testing compound; 2) detecting all types of signals that are produced by all of possible protein-compound interactions, in the claimed methods, because the specification does not establish: (A) regions of the protein structure which may be modified without affecting its desired activity, i.e., compound-binding activity, or kinase activity; (B) adequate guidance with respect to the type of signal a skilled artisan should look for upon carrying out the claimed methods; (C) the general tolerance of the protein to modification and extent of such tolerance, especially with respect to the region of the protein that mediates the protein-compound interactions or the catalysis of phosphorylation; (D) a rational and predictable scheme for modifying any amino acid residue of the protein with an expectation of obtaining the desired biological function; and (E) the specification provides insufficient guidance as to which of the essentially infinite possible choices is likely to be successful.

Because of this lack of guidance, and the fact that the relationship between the polypeptide sequence of a protein and its activity/function is not well understood and unpredictable (e.g., see Ngo et al. in The Protein Folding Problem and Tertiary Structure Prediction, 1994, Merz et al. (ed.), Birkhauser, Boston, MA, pp. 433 and 492-

495, Ref: U, Form-892), it would require undue experimentation for one skilled in the art to make and use the claimed methods.

The scope of the claims must bear a reasonable correlation with the scope of enablement (In re Fisher, 166 USPQ 19 24 (CCPA 1970)). Without sufficient guidance, determination of any protein encoded by any T17E9.1a/*kin-18* gene or any ortholog thereof having the desired biological characteristics is unpredictable and the experimentation left to those skilled in the art is unnecessarily, and improperly, extensive and undue. See In re Wands 858 F.2d 731, 8 USPQ2nd 1400 (Fed. Cir, 1988).

Claim Rejections - 35 U.S.C. § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. § 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 18-29 are rejected under 35 U.S.C. § 102(b) as being anticipated by Tassi et al. (Human JIK, a novel member of the STE20 kinase family that inhibits JNK and is negatively regulated by epidermal growth factor, Journal of Biological Chemistry, 1999, 274(47): 33287-33295).

The instant claims are drawn to a method for identifying a compound useful in the prevention and/or treatment of metabolic diseases, comprising the steps of: a)

contacting a protein or polypeptide encoded by a T17E9.1a/*kin-18* gene or an ortholog thereof with a test chemical, in such a way that a signal is generated that is representative for the interaction between said test chemical and said protein or polypeptide; and b) detecting the signal thus generated, said signal identifying a compound that modulates said protein or polypeptide, which is indicative that the compound is useful for the prevention and/or treatment of metabolic diseases.

Tassi et al. teach that human JNK/SAPK-inhibitory kinase, JIK, is a novel member of the STE20 kinase family that inhibits JNK, and is negatively regulated by epidermal growth factor. Tassi et al. specifically teach a method, comprising the steps of: a) contacting human JIK protein (identical to SEQ ID NO: 4, see Figure 1A) encoded by human *JIK* gene, which is an ortholog of T17E9.1a/*kin-18,* with test chemicals such as, anisomycin, NaCl, or H_2O_2, so that a signal, γ-^{32}P isotope-labeled kinases, are produced by the kinase activity of JIK proteins, that is representative of the interaction between said test chemical and said protein. The taught method further comprises detecting a signal generated by the autoradiography, which indicates whether the kinase activity of JIK protein has been increased or decreased compared to the controls (see pg. 33288, under sections "Immunoprecipitation and autophosphorylation assay," "MAPK assays," and "Phosphoamino Acid Analysis"; and the results of Figures 4, 5, 6 and 7 on pgs. 33291-33293), thereby anticipating Applicant's claims 18-23. Tassi et al. further teach the transfection of human *JIK* gene in COS7 cells and carrying out aforementioned assays, thereby anticipating Applicant's claims 24-29.

Therefore, Tassi et al. anticipate the Applicants' claimed methods.

Conclusion

Claims 18-29 are rejected for the reasons as stated above. Applicants must respond to the objections/rejections in each of the numbered sections in this Office action to be fully responsive in prosecution.

The instant Office action is non-final.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jae W. Lee whose telephone number is 571-272-9949. The examiner can normally be reached on 8:00-4:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Kathleen K. Bragdon can be reached on 571-272-0931. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

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PRIMARY EXAMINER